

This listing of the claims will replace all prior versions, and listings, of claims in the application:

LISTING OF THE CLAIMS

Claim 1 (Currently amended): A method for synthesizing isopentenyl pyrophosphate in a host microorganism, wherein the method comprises introducing into the host microorganism a plurality of heterologous nucleic acid sequences, each coding for a different enzyme in the mevalonate pathway for producing isopentenyl pyrophosphate, and culturing the host microorganism in the presence of a suitable medium, wherein the synthesis comprises the steps of (a) condensing two molecules of acetyl-CoA to acetoacetyl-CoA; (b) condensing acetoacetyl-CoA with acetyl-CoA to form HMG-CoA; (c) converting HMG-CoA to mevalonate; (d) phosphorylating mevalonate to mevalonate 5-phosphate; (e) converting mevalonate 5-phosphate to mevalonate 5-pyrophosphate; and (f) converting mevalonate 5-pyrophosphate to isopentenyl pyrophosphate.

Claim 2 (Original): The method of claim 1, wherein the plurality of heterologous nucleic acid sequences is integrated into the chromosome of the host microorganism.

Claim 3 (Original): The method of claim 1, wherein the plurality of heterologous nucleic acid sequences is contained in at least one extrachromosomal expression vector.

Claim 4 (Original): The method of claim 3, wherein the plurality of heterologous nucleic acid sequences is present in a single expression vector.

Claim 5 (Original): The method of claim 4, wherein the single expression vector contains the nucleotide sequence SEQ ID NO 7.

Claim 6 (Original): The method of claim 3, wherein each heterologous nucleic acid sequence is contained within a different expression vector.

Claim 7 (Original): The method of claim 3, wherein at least two of the heterologous nucleic acid sequences are contained in a single expression vector.

Claim 8 (Original): The method of claim 3, wherein some of the heterologous nucleic acid sequences are contained in a first expression vector, and the remainder of the sequences, in a second expression vector.

Claim 9 (Original): The method of claim 8, wherein the first expression vector contains the nucleotide sequence SEQ ID NO 8, and the second expression vector includes the nucleotide sequence contained in SEQ ID NO 9.

Claim 10 (Original): The method of claim 1, wherein the plurality of heterologous nucleic acid sequences comprises:

- a) a DNA fragment coding for an enzyme capable of condensing two molecules of acetyl-CoA to acetoacetyl-CoA;
- b) a DNA fragment coding for an enzyme capable of condensing acetoacetyl-CoA with acetyl-CoA to form HMG-CoA;
- c) a DNA fragment coding for an enzyme capable of converting HMG-CoA to mevalonate;
- d) a DNA fragment coding for an enzyme capable of phosphorylating mevalonate to mevalonate 5-phosphate;
- e) a DNA fragment coding for an enzyme capable of converting mevalonate 5-phosphate to mevalonate 5-pyrophosphate; and
- f) a DNA fragment coding for an enzyme capable of converting mevalonate 5-pyrophosphate to isopentenyl pyrophosphate.

Claim 11 (Original): The method of claim 10, wherein the plurality of individual heterologous nucleic acid sequences comprises:

- a) the nucleotide sequence of SEQ ID NO 1;
- b) the nucleotide sequence of SEQ ID NO 2;

- c) the nucleotide sequence of SEQ ID NO 3;
- d) the nucleotide sequence of SEQ ID NO 4;
- e) the nucleotide sequence of SEQ ID NO 5; and
- f) the nucleotide sequence of SEQ ID NO 6.

Claim 12 (Original): The method of claim 1, wherein the isopentenyl pyrophosphate is recovered from the host microorganism.

Claim 13 (Currently amended): The method of claim 1, wherein the at least one isopentenyl pyrophosphate is reacted with dimethylallyl pyrophosphate or a polyprenyl pyrophosphate in the presence of at least one enzyme further modified to provide a polyprenyl pyrophosphate isoprenoid precursor, which is then reacted in the presence of an enzyme to form an isoprenoid.

Claim 14 (Original): The method of claim 13, wherein the plurality of heterologous nucleic acid sequences further comprises:

g) a DNA fragment coding for an enzyme capable of converting isopentenyl pyrophosphate to dimethylallyl pyrophosphate.

Claim 15 (Original): The method of claim 13, wherein the isoprenoid is selected from the group consisting of a monoterpane, sesquiterpene, diterpene, sesterterpene, triterpene, tetraterpene, and a steroid.

Claim 16 (Original): The method of claim 15, wherein the isoprenoid is a monoterpane.

Claim 17 (Original): The method of claim 16, wherein the monoterpane is selected from the group consisting of limonene, citraneolol, and geraniol.

Claim 18 (Original): The method of claim 15, wherein the isoprenoid is a sesquiterpene.

Claim 19 (Original): The method of claim 18, wherein the sesquiterpene is selected from the group consisting of periplanone B, artemisinin, ginkgolide B, forskolin, and farnesol.

Claim 20 (Currently amended): The method of claim 15, wherein the isoprenoid is a diterpene.

Claim 21 (Original): The method of claim 20, wherein the diterpene is selected from the group consisting of casbene and paclitaxel.

Claim 22 (Original): The method of claim 1, wherein the host microorganism is a prokaryote.

Claim 23 (Original): The method of claim 22, wherein the prokaryote is *Escherichia coli*.

Claim 24 (Withdrawn): A method for synthesizing isopentenyl pyrophosphate in a host microorganism, wherein the method comprises introducing into the host microorganism an intermediate in the mevalonate pathway and at least one heterologous nucleic acid sequence, each said sequence coding for an enzyme in the mevalonate pathway necessary for converting the intermediate into isopentenyl pyrophosphate.

Claim 25 (Withdrawn): The method of claim 24, wherein a plurality of heterologous nucleic acid sequences is introduced into the host microorganism.

Claim 26 (Withdrawn): The method of claim 25, wherein the plurality of heterologous nucleic acid sequences is integrated into the chromosome of the host microorganism.

Claim 27 (Withdrawn): The method of claim 25, wherein the plurality of heterologous nucleic acid sequences is contained in at least one extrachromosomal expression vector.

Claim 28 (Withdrawn): The method of claim 27, wherein the plurality of heterologous nucleic acid sequences is present in a single expression vector.

Claim 29 (Withdrawn): The method of claim 28, wherein the expression vector includes the nucleotide sequence contained in SEQ ID NO 9.

Claim 30 (Withdrawn): The method of claim 25, wherein the intermediate is DL-mevalonate and the plurality of heterologous sequences comprises:

- a) a DNA fragment coding for an enzyme capable of phosphorylating mevalonate to mevalonate 5-phosphate;
- b) a DNA fragment coding for an enzyme capable of converting mevalonate 5-phosphate to mevalonate 5-pyrophosphate; and
- c) a DNA fragment coding for an enzyme capable of converting mevalonate 5-pyrophosphate to isopentenyl pyrophosphate.

Claim 31 (Withdrawn): The method of claim 30, wherein the plurality of individual heterologous nucleic acid sequences comprises:

- a) the nucleotide sequence of SEQ ID NO 4;
- b) the nucleotide sequence of SEQ ID NO 5; and
- c) the nucleotide sequence of SEQ ID NO 6.

Claim 32 (Withdrawn): The method of claim 24, wherein the isopentenyl pyrophosphate is recovered from the host microorganism.

Claim 33 (Withdrawn): The method of claim 25, wherein the plurality of heterologous nucleic acid sequences further comprises:

- g) a DNA fragment coding for an enzyme capable of converting isopentenyl pyrophosphate to dimethylallyl pyrophosphate.

Claim 34 (Withdrawn): The method of claim 24, wherein the isopentenyl pyrophosphate is further modified to provide an isoprenoid.

Claim 35 (Withdrawn): The method of claim 34, wherein the isoprenoid is selected from the group consisting of a monoterpene, sesquiterpene, diterpene, sesterterpene, triterpene, tetraterpene, and a steroid.

Claim 36 (Withdrawn): The method of claim 35, wherein the isoprenoid is a monoterpene.

Claim 37 (Withdrawn): The method of claim 36, wherein the monoterpene is selected from the group consisting of limonene, citranellol, and geraniol.

Claim 38 (Withdrawn): The method of claim 35, wherein the isoprenoid is a sesquiterpene.

Claim 39 (Withdrawn): The method of claim 38, wherein the sesquiterpene is selected from the group consisting of periplanone B, artemisinin, ginkgolide B, forskolin, and farnesol.

Claim 40 (Withdrawn): The method of claim 35, wherein the isoprenoid is a diterpene.

Claim 41 (Withdrawn): The method of claim 40, wherein the diterpene is selected from the group consisting of casbene and paclitaxel.

Claim 42 (Withdrawn): The method of claim 24, wherein the host microorganism is a prokaryote.

Claim 43 (Withdrawn): The method of claim 42, wherein the prokaryote is *Escherichia coli*.

Claim 44 (Withdrawn): An isolated DNA fragment coding for the enzymes in the mevalonate pathway for producing isopentenyl pyrophosphate.

Claim 45 (Withdrawn): The isolated DNA fragment of claim 44, comprising the nucleotide sequence of SEQ ID NO 7.

Claim 46 (Withdrawn): An expression vector comprising the DNA fragment of claim 44.

Claim 47 (Withdrawn): The expression vector of claim 46, wherein the DNA fragment comprises the nucleotide sequence of SEQ ID NO 7.

Claim 48 (Withdrawn): A host cell transformed with the expression vector of claim 46.

Claim 49 (Withdrawn): An isolated DNA fragment coding for a fraction of the enzymes in the mevalonate pathway for producing isopentenyl pyrophosphate comprising the nucleic acid sequences comprised of:

- a) a DNA fragment coding for an enzyme capable of condensing two molecules of acetyl-CoA to acetoacetyl-CoA;
- b) a DNA fragment coding for an enzyme capable of condensing acetoacetyl-CoA with acetyl-CoA to form HMG-CoA; and
- c) a DNA fragment coding for an enzyme capable of converting HMG-CoA to mevalonate.

Claim 50 (Withdrawn): The DNA fragment of claim 49, comprising the nucleotide sequence of SEQ ID NO 8.

Claim 51 (Withdrawn): An expression vector comprising the DNA fragment of claim 49.

Claim 52 (Withdrawn): The expression vector of claim 51, comprising the nucleotide sequence of SEQ ID NO 8.

Claim 53 (Withdrawn): A host cell transformed with the expression vector of claim 51.

Claim 54 (Withdrawn): An isolated DNA fragment coding for a fraction of the enzymes in the mevalonate pathway for producing isopentenyl pyrophosphate comprising the nucleic acid sequences comprised of:

- a) a DNA fragment coding for an enzyme capable of phosphorylating mevalonate to mevalonate 5-phosphate;
- b) a DNA fragment coding for an enzyme capable of converting mevalonate 5-phosphate to mevalonate 5-pyrophosphate; and
- c) a DNA fragment coding for an enzyme capable of converting mevalonate 5-pyrophosphate to isopentenyl pyrophosphate.

Claim 55 (Withdrawn): The DNA fragment of claim 54, comprising the nucleotide sequence of SEQ ID NO 9.

Claim 56 (Withdrawn): An expression vector comprising the DNA fragment of claim 54.

Claim 57 (Withdrawn): The expression vector of claim 55, comprising the nucleotide sequence of SEQ ID NO 9.

Claim 58 (Withdrawn): A host cell transformed with the expression vector of claim 56.

Claim 59 (Withdrawn): A host cell transformed with a first expression vector containing some of the heterologous nucleic acid sequences coding for enzymes in the mevalonate pathway for producing isopentenyl pyrophosphate contained in a first expression vector, and the remainder of the sequences, in a second expression vector.

Claim 60 (Withdrawn): The host cell of claim 59, wherein the first expression vector contains the nucleotide sequence of SEQ ID NO 8 and the second expression vector contains the nucleotide sequence of SEQ ID NO 9.